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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,558	03/25/2005	Ernst Hafen	27656/38365A	1027

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EXAMINER	
EMCH, GREGORY S	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 03/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/509,558	HAFEN ET AL.	
	Examiner	Art Unit	
	Gregory S. Emch	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *1-5 and 13-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Formal Matters

Claims 6 and 9 were amended in the Response filed 23 December 2005. Claims 1-27 are pending. Claims 1-5 and 13-27 were previously withdrawn from consideration as drawn to non-elected inventions. Currently, claims 6-12 are under consideration.

Response to Amendments/Arguments

The objection to claim 9 is withdrawn in response to Applicants' amendment of said claim, as set forth in the Response filed 23 December 2005.

The enablement rejection of claims 6-12 under 35 U.S.C. 112, first paragraph is withdrawn in response to Applicants' arguments, as set forth in the Response filed 23 December 2005.

The rejection of claims 6-12 under 35 U.S.C. 112, second paragraph is withdrawn in response to Applicants' amendment of claim 6, as set forth in the Response filed 23 December 2005.

New are set forth below.

The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Claim Rejections - 35 USC § 112, first paragraph

Claims 6-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The specification as originally filed does not provide support for the invention as now claimed: "and correlating said change in expression level, mutation or rearrangement with a standard indicative of a hyperproliferative disease to determine the occurrence of a hyperproliferative disease." The specification as filed does not provide a written description or set forth the metes and bounds of this phrase. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the written description requirement of the first paragraph of 35 U.S.C. 112.

Applicants are required to cancel the new matter in the response to this Office action. Alternatively, Applicants are invited to provide the location in the specification of sufficient written support for the "limitation" indicated above. (Please note that this issue could be overcome by amending the claims to recite, for example, "wherein said change in expression level, mutation or rearrangement is indicative of hyperproliferative disease").

Claims 6-12 are also rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of the identification of a hyperproliferative disease, which comprises detecting a change in ELP mRNA or protein expression levels from a tissue sample, does not reasonably provide enablement for a method of the identification of a hyperproliferative disease in a body fluid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 6-12 are directed to a method for the identification of a hyperproliferative disease, which comprises detecting in a body fluid or a tissue sample of a subject in need thereof a change in the expression level of an ELP protein or at least one mutation within a nucleic acid sequence encoding an ELP protein or detecting a rearrangement in the genomic *elp* locus and correlating said change in expression level, mutation or rearrangement with a standard indicative of a hyperproliferative disease to determine the occurrence of a hyperproliferative disease.

The specification at p. 35, line 33 – p. 36, line 22 (Example XI and Table 3) discloses ELP RNA expression in normal vs. tumor tissues. Here, reductions in human ELP mRNA expression compared with their respective normal tissues were observed in the majorities of lung, kidney, and stomach cancer samples.

Applicants do not disclose any actual or prophetic examples on expected performance parameters involving any bodily fluid sample. Applicants have only disclosed methods involving measuring a downregulation of mRNA expression of hELP

in lung, kidney, and stomach cancer tissue samples. As such, the art teaches that identifying cancer from bodily fluids, such as blood is unpredictable. The instant invention relies on the recognition of antigens or gene transcripts that are expressed only by tumor cells and not by surrounding cells. However, relevant art regarding stomach cancer teaches that it is often difficult to find such an antigen because those expressed by the primary tumor cell may have been downregulated or lost (Vogel et al. Virchows Arch 439:109-117, 2001). Vogel et al. teaches that it is assumed that disseminated tumor cells of non-haematopoietic origin normally do not circulate in the peripheral blood (p.110, paragraph 7).

Furthermore, Skates et al. (Clin Cancer Res 10:6296S-301S, 2004) teaches that even if a biomarker for renal cell carcinoma was extremely sensitive and had an extremely high specificity, the positive predictive value would still be low and "achieving such an exacting combination of sensitivity and specificity is unlikely for a blood test" (p.6296s, para.4). Skates et al. also teaches that further testing i.e. more expensive imaging tests, would be needed to validate the findings of a blood test (para.4).

In addition, Bunn (J Clin Oncol 21(21):3891-3, 2003) teaches that studies of serum protein markers for lung cancer failed to produce sufficient sensitivity or specificity for routine use (p.3891, para.1). Bunn also teaches that although some studies have shown that DNA markers for cancer are present in the serum, "much remains to be done before these tests become standard (para.2). Accordingly, Bunn presents a diversity of findings between studies evaluating serum plasma markers in lung cancer patients (p.3892, Table 1) reflecting the unpredictability of such an assay.

Bunn concludes, "for lung cancer, much needs to be done in validation, and much larger series must be completed before these tests are ready for prime time" (p.3893). Further, Shaw et al. (Clin Cancer Res. 11(13 Pt 2): 4999s-5003s, 2005) teaches, "no reliable circulating biomarkers of lung cancer have been identified that allow early diagnosis" (Abstract). Shaw et al. also teaches that although mouse models of lung cancer show some promise, "before any biomarkers can enter into clinical practice, they will need to be validated in patient samples" and in clinical trials (5003s).

Furthermore, the prior art discussed *supra* does not address bodily fluid samples other than blood or serum. For example, while it may be possible to detect bladder cancer from urine samples and lung cancer from sputum, it is unclear how stomach cancer would be detected from urine. Similarly, how would the artisan detect breast cancer from saliva? Such details are missing from Applicants' disclosure. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. Due to the large quantity of experimentation necessary to establish a nexus between detecting a change in the expression level of an ELP protein, a mutation in a nucleic acid sequence encoding an ELP protein, or a rearrangement in the genomic *elp* locus in any bodily fluid and the identification of a hyperproliferative disease, given the lack of direction/guidance presented in the specification, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the claimed methods, and the breadth of the claims which encompass changes in protein expression and in nucleic acid expression in bodily fluids and tissue samples, undue

experimentation would be required of the skilled artisan to practice the claimed invention commensurate with the scope of the claims.

Conclusion

No claims are allowable.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gregory S. Emch whose telephone number is (571) 272-8149. The examiner can normally be reached on Monday through Friday from 8:30AM to 5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gregory S. Emch, Ph. D.
Patent Examiner
Art Unit 1649
March 13, 2005

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER